deficiencies pointed out in the Action, under 35 U.S.C. §112. Applicant's attorney apologizes for any inconvenience because of these informalities. Claims 1-21 and 23-24 are amended. New claim 25 is added. Applicant's attorney is very grateful to Examiner Zeman for her assistance in clarifying the complexities in this case.

The Action rejects claims 1-4 and 21-24 as being anticipated under 35 U.S.C. 102(e) by: 1) Armstrong et al. (U.S. Patent No. 6,099,469) and by 2) Carlson et al. (U.S. Patent No. 6,140,065) claims 1-4, 21-24, 12 and 18 under 35 U.S.C. 102(b) and by 3) Sreevatsan et al. (Journal of Clinical Biol. 1998, 36: 1895-1901). In response, applicant disagrees with these rejections based on the three cited references, for the reasons that follow:

Armstrong et al. U.S. Patent No. 6,099,469

The Action states that Armstrong et al. discloses a disease specific algorithm for use in a computer assisted method, which analyzes what clinical tests should be performed for acute myocardial infarction. A first test is performed on a sample, then, based upon the result of that test in comparison with preset guidelines, a second test is run. The process is repeated until an endpoint ----the diagnosis of a condition --- is reached (col. 4-11). Figures 1B-1F set forth in the decision tree of clinical tests and diagnoses, and Figure 2 plus the discussion from col. 11, line 30 to col. 14, line 25, set forth the apparatus.

In response, Applicant concurs that Armstrong et al. describes a computer assisted method comprising a sequential process of testing biomarkers for myocardial infarction by a reflex algorithm, for use in the early diagnosis of acute myocardial infarction. However, Armstrong et al.'s reflex algorithm and its application in the diagnosis of myocardial infarction can be distinguished from the present invention. In fact, the present invention would be entirely non-enabling if applied in the diagnosis of myocardial infarction for the following reasons:

A. Armstrong et al.'s reflex algorithm is used to monitor a number of biochemical markers, which change in a time-sensitive manner during a myocardial infarction episode, for example creatinine kinase, myoglobin and troponin. These time dependent changes in the specific biomarkers are monitored by a technician in order to determine the stage at which the myocardial infarction is being monitored. And, sometimes, this requires that the same biomarker test be run repeatedly every four hours in order to follow the progression of the myocardial infarct. In other words, it is the technician who decides as to whether to repeat any testing. The reflex algorithm merely indicates how a measurement for a biomarker compares with a predetermined level.

In contrast, in the present invention, the algorithmic clinical testing allows a technician to load a sample and rely on a specific algorithm to execute the necessary tests in a sequential manner, to obtain an accurate diagnosis. The system is not time sensitive and as mentioned above, would be unsuitable to diagnose early phase of

myocardial infarction because, once a test has shown to be negative, it is not repeated at intervals to see if it will turn to positive. The objective in the present invention is to provide a cost-effective system that can be used in the diagnosis of many diseases in which the markers being measured have stable values. The system is capable of carrying out intelligent programming to effectuate diagnosis and does not need the technician to make the decisions as is the case in Armstrong et al.

B. Armstrong et al. describes methods and systems for diagnosing myocardial infarction in an emergency or cardiac unit, where cost is not a factor. What is important is accuracy of diagnosis and the system provides reflex algorithms which follow biomarker changes which are time sensitive in relation to the myocardial infarct onset.

In contrast, the present invention addresses the problem of cost, efficiency and accuracy in clinical testing, often times in clinical laboratories and not in hospital wards. The present invention comprises of methods and systems which employ disease-specific algorithms, and provide cost effective, efficient, accurate and complete diagnostic information, and cut out the unnecessary tests. In fact, a test found to be negative is not repeated unless if it is suspected of experimental error.

C. Armstrong et al. describes a method for diagnosis of acute myocardial infarction in which the biomarker measurement performed based on results from a

precedent biochemical marker measurement step, is repeated at one of a plurality of different times subsequent to submission --- col. 17, lines 14-18.

In contrast, the present invention provides an algorithmic clinical testing system using intelligent programming aimed at automated laboratory cost-cutting.

"It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention". *Hybritech Inc. v. Monoclonel Antibodies Inc.* 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986).

Therefore, as a matter of law and fact, the rejection of claims 1-4 and 21-24 based on Armstrong et al. should be withdrawn.

2. Carson et al., U.S. Patent No. 6,140,065

The Action cites Carson et al. as disclosing computer assisted methods for differently diagnosing benign prostate disease and prostate adencarcinomas. The diagnostic method comprises five (5) steps of measuring total PSA, free PSA, factoring in age and applying the algorithm $PV\text{-}P_1/(1\text{-}P_1)$. The free PSA measurements are done only if total PSA is between about 4.0 to 20.0 ng lmL.

In response, applicant describes a prostate cancer algorithm, in which the total PSA of < 4.0 is negative, of 4 to 9.9 is equivocal (and requires measurement of free PSA) and > 10 is positive (and requires measurement of serum bone marker). Therefore, the prostate algorithm of the present invention is different and can be

distinguished from that of Carson et al. The rejection of claims 1-4 and 21-24 should be withdrawn.

3. Sreevatsan et al., J. Clin Micro. 1998, 36:1895-1901

The Action states that the present invention is anticipated by Sreevatsan et al., because the cited reference discloses reflex algorithms for the different diagnoses of Hepatitis C Virus stereotypes, and Figure 3 as setting forth the decision tree to be used in the process.

Applicants disagree with this rejection.

> "For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference - - - These elements must be arranged as in the claim under review, - - - ." *In re Bond*, 910 F.2d 831, 15 USPQ 1566 (Fed. Cir. 1990)."

Sreevatsan et al. describes an algorithm approach to high-throughput molecular screening for alpha interferon-resistant genotypes for HCV detection. The study was designed to validate use of Cleavage Fragment Length Polymorphism (CFLP) analysis as an alternative to DNA sequencing for high-throughput screening of HCV genotypes in a high-volume molecular pathology laboratory setting. (emphasis added Refer to

Abstract). Thus, Sreevatsan et al. describe an algorithm that is suitable for use after the application of the algorithm for hepatitis of the present invention in a routine clinical laboratory. Clearly the elements for the Sreevatsan et al. algorithm for HCV genotypes and the elements for the hepatitis algorithm are different in all ways – in methodology, in decision making dependent on results of a preceding test, in interferon – resistance, etc.

Therefore, there is no basis as a matter of fact and law, pursuant to *In re Bond*, for the rejection of claims 1, 2 and 3 based on Sreevatsan. Applicant, respectfully requests that this rejection be withdrawn.

Applicant has made a diligent effort to place this application in condition for allowance and notice to the effect that claims 1-21 and 23-25 are in condition for allowance is earnestly solicited.

If for any reason however, the Examiner should deem that this application is not in condition for allowance, the Examiner is respectfully requested to telephone the undersigned attorney at the number listed below to resolve any outstanding issues prior to issuing a further Office Action.

Respectfully submitted,

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I hereby certify that this correspondence is being sent via Express Mail No. EK907853498US to the United States Patent and Trademark Office, Washington, D.C. 20231 and a courtesy copy is being transmitted via facsimile at **(703) 308-8724** to Examiner Mary K. Zeman on June 13, 2001.

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Signature

June 13, 2001

Date of Signature